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(54) Title: LOW ODOR CHOLINE SALTS

(57) Abstract

A low-odor choline salt purified to an extent wherein the equilibrium concentration of trimethylamine in the atmosphere above the choline salt is less than 0.2 parts per billion.

TITLE

LOW ODOR CHOLINE SALTS

FIELD OF THE INVENTION

The invention is directed to a low odor choline salt product. More particularly, the invention is directed to a choline salt product which does not release an amine or "fishy-like" odor, due to a reduction in the content of total trimethylamine in the choline salt by purification.

BACKGROUND OF THE INVENTION

Choline is a dietary component that is important for the structural integrity of cell membranes, methyl metabolism, cholinergic neurotransmission, transmembrane signaling, and lipid-cholesterol transport and metabolism. Choline accelerates the synthesis and release of acetylcholine, an important neurotransmitter involved in memory storage, muscle control, and many other functions. Choline is also a precursor for the synthesis of (1) phospholipids including phosphatidylcholine, a membrane constituent important for the structure and function of membranes, for intracellular signaling, and for hepatic support of very low-density lipoproteins; (2) sphingomyelin, another membrane constituent that has structural and signaling functions; and (3) platelet activating factor, a potent messenger molecule. Finally, choline is a precursor for the formation of the methyl donor betaine.

Choline has been used widely in a number of applications for many years. Its predominant use is in the animal nutrition field, and, in the form of chloride salt, it is used as a direct dietary supplement for production animals such as poultry, swine and the like. Choline also has application in the human nutrition field, where several salts of choline are used to convey this nutrient into the diet. In 1998, the U.S. Institute of Medicine published a recommendation for adequate intake of choline in the human diet. It is recognized as an essential nutrient in both humans and animals, and has been used commercially for nearly 50 years. The primary functions of choline are (1) nerve transmission; (2) as a component of cell membranes; (3) as a lipotropic (fat metabolizing) agent where it helps to prevent liver damage; and (4) as a methyl group donor in the production of DNA

and the odor is often offensive enough to cause people to avoid such choline containing products. The source of this odor can actually be traced to trimethylamine (TMA) salt impurities remaining in the product after its manufacture. It is Applicants' discovery that the TMA salt impurities in a choline salt can be reduced to a low enough level that the choline salt does not emit a detectable amine or "fishy" odor.

Choline salts are produced by reaction of TMA with ethylene oxide or ethylene chlorohydrin and an acid, such as hydrochloric, tartaric, citric, etc. As with any synthesis, natural or otherwise, the final product is rarely of such purity as to exclude all other ingredients or byproducts. TMA salt is often found as an impurity in choline salts, resulting from incomplete raw material conversion. The TMA salt in the choline salt is in equilibrium with free TMA, releasing into the atmosphere a very low level of volatile (free) TMA, but enough to exceed the odor threshold for humans. TMA is widely recognized as having a strong amine-like, fishy odor, detectable by humans at levels as low as 0.2 parts per billion (ppb) in air.

It is a primary objective of this invention to provide a choline salt product which does not emit this characteristic amine-like odor. In particular, when a choline salt product is packaged in container for sale to a customer, it is preferred that the packaged choline does not emit the amine-like odor when the container is opened. Therefore, it is preferred that the choline salt product of the invention be purified to an extent wherein the equilibrium concentration of TMA in the atmosphere above the choline salt is less than 0.2 parts per billion.

The concentration of volatile (free) TMA in equilibrium with the salts in the choline salt product is dependent on a number of factors, including temperature, humidity, and most importantly, the acidity of the TMA salt. In particular, the free amine concentration will depend on the ratio of TMA groups to acid. Therefore, in the case of a polycarboxylic acid, such as tartaric acid, wherein the acid salt is TMA tartrate (which contains 2 moles of amine per mole of tartaric acid), it can be expected that the product will release orders of magnitude more free TMA than would TMA bitartrate, the amine and acid components of which

$$CaCO_3 + Ch^+ TartH^- \rightarrow CaTart + Ch^+ HCO_3^-$$

If a TMA salt is present, even at relatively low levels, an analogous reaction will occur, yielding free TMA:

$$CaCO_3 + Me_3NH^+ TartH^- \rightarrow CaTart + Me_3NH^+ HCO_3^-$$

$$\downarrow$$

$$Me_3N + CO_2 + H_2O$$

This reaction is a non-equilibrium process, which will rapidly release into the atmosphere much of the TMA content of the salt. Thus, if the application involves use of choline salts in the presence of an alkaline ingredient, it is even more critical that the level of TMA salt impurities be as low as possible. This is perhaps one of the most important advantages of our low-TMA choline salts.

The advantageous properties of this invention can be observed by reference to the following examples which illustrate the invention.

EXAMPLES

EXAMPLE 1

Purification by Crystallization

A 250 g. sample of choline bitartrate containing 45 ppm of TMA (as the bitartrate salt) was charged to 375 mL of water and heated with stirring until completely dissolved. Water was then removed in vacuo using a rotary evaporator, until crystals appeared and became heavy, at which point 250 mL of methanol was charged to the slurry. The mixture was cooled to ~3 °C and held for one hour. The crystalline product was then filtered, washed on the funnel with ~50 mL of cold methanol and dried, to yield a product containing 5 ppm of trimethylamine (as the bitartrate salt). This resulting product having 5 ppm of total trimethylamine did not emit a detectable level of characteristic amine or "fishy" odor normally associated with choline bitartrate.

TITLE

LOW ODOR CHOLINE SALTS

CLAIMS

We Claim:

1. A low odor choline salt product purified to an extent wherein the equilibrium concentration of trimethylamine in the atmosphere above the choline salt is less than 0.2 parts per billion.

2. The choline salt product of claim 1 wherein the choline salt product is disposed within a sealable container.

3. The choline salt product of claim 1 wherein the choline salt is selected from the group consisting of choline bitartrate, choline dihydrogen citrate and choline chloride.

4. The choline salt product of claim 1 further comprising an alkaline ingredient.

5. The choline salt product of claim 4 wherein the choline salt is selected from the group consisting of choline bitartrate, choline dihydrogen citrate and choline chloride.

6. The choline salt product of claim 5 further comprising less than 10 parts per million of trimethylamine.

7. The choline salt product of claim 6 further comprising less than 5 parts per million of trimethylamine.

8. A low odor choline salt product selected from the group consisting of choline bitartrate, choline dihydrogen citrate and choline chloride, wherein the